## Note

# The reaction of resonance-stabilized ylids with D-ribose and D-glucose derivatives<sup>1</sup>

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## INTRODUCTION

Recently, we reported<sup>2</sup> the preparation of intermediates for the total synthesis of the antibiotic Showdomycin by the reaction of ylids of maleimide with derivatives of D-ribose. As an extension of this work, we prepared a number of ylids that are resonance-stabilized by a variety of electron-withdrawing groups (such as ester, amide, imide, and nitrile) and studied their reaction with D-glucose and D-ribose derivatives. In the past, Wittig reactions involving resonance-stabilized ylids have been used for preparing useful intermediates for the synthesis of several unsaturated and long-chain carbohydrates<sup>3</sup>. Both protected and unprotected monosaccharides have been used in these reactions<sup>4</sup>. The reaction of resonance-stabilized ylids with carbohydrates is generally quite simple and affords high yields of the Wittig reactionproducts. The failure to isolate any products in certain of the reactions is, perhaps, attributable to competing reactions, such as the aldol reaction (catalyzed by the basic ylids) or the reaction of the ylid with the protecting groups on the carbohydrate<sup>5</sup>.

## RESULTS AND DISCUSSION

In order to determine the relative reactivity of various ylids with carbohydrates containing different protecting groups, seven stabilized ylids were prepared. (Triphenylphosphoranylidene)succinimide (1) and its *N*-phenyl derivative 2 were prepared by treating triphenylphosphine with maleimide and *N*-phenylmaleimide, respectively, by the procedure of Heyda and Theodoropulos<sup>6</sup>. The ylids 3–7 were prepared by the dehydrohalogenation of the corresponding phosphonium salts<sup>7</sup>. 2,4:3,5-Di-O-benzylidene-aldehydo-D-ribose (8) was prepared by the procedure of Potgieter and MacDonald<sup>8</sup>, and penta-O-acetyl-aldehydo-D-glucose (9) was obtained as described by Wolfrom and Thompson<sup>9</sup>. The aldehydo sugars 8 and 9 were separately treated with each of the ylids 1–7 and the results are summarized in Table I. The D-ribose derivative 8 reacted with all of the ylids and gave the expected Wittig reaction-products

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# TABLE I

PRODUCTS FROM THE REACTION OF RESONANCE STABILIZED YLIDS WITH DERIVATIVES OF (A) D-RIBOSE AND (B) D-GLUCOSE

Ylida	Product <sup>b</sup> (A)	Yield (%)	Product <sup>c</sup> (B)	Yield (%)
	R'CH NH 10	86	intractable mixture	
	R'CH N-Ph	8 <i>5</i>	intractable mixture	
⊖ ∥ R—CH—C—№ 3	O    IH2 R'CH=CHCNH2 12	64	0    R*CH=CHCNH2 17	55
⊖ ∥ RCHC0 4	O    DEt R'CH=CHCOEt 13	75	O ∥ R*CH=CHCOEt 18	80
⊖ RCHCN 5	R'CH=CHCN 14	60	R″CH≃CHCN 19	48
0 ⊖ ∥ R—CH—C—M 6	O    le R'CH=CHCMe 15	82	no reaction	
O ⊖ ∥ R—CH—CPh 7	O    R'CH=CHCPh 16	63	O    R*CH=CHCPh 20	57
$^{a}R = \stackrel{\oplus}{P}(Pn)_{3}$			$= H_2 C - C - C - C - C - C - C - C - C - C $	

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10-16. The reaction between the respective ylids 3, 4, 5, and 7 and the D-glucose derivative 9 afforded products 17-20, respectively. However, compound 9 did not react with ylid 6, and, with ylids 1 and 2, it afforded intractable, complex mixtures.



The resonance structures 21-23 can be considered to represent the stabilized phosphonium ylids. The greater the charge localization on the carbon atom (as shown in structure 21), the more basic (and, presumably, more nucleophilic) should the ylid



be<sup>10</sup>. Thus, an increase in the  $pK_a$  of the ylid should increase its reactivity. Likewise, the carbonyl band in the infrared spectrum of the ylid should show a marked shift to longer wavelengths as such structures as 22 become more important. Hence, it would be expected that the relative basicities and the shifts in the carbonyl stretching frequency of the ylids would be good measures of the relative reactivities of a particular series of ylids.

In 1963, Speziale and Ratts<sup>10</sup> attempted, for a series of resonance-stabilized halo-ylids, to correlate the reactivity to their basicity and to the carbonyl stretching frequency in their infrared spectra. However, their results were insufficiently conclusive to permit any structure-reactivity correlations for the halo-ylids. In an attempt to explain the observed differences in the reactivity of the ylids 1–7 with the D-ribose and D-glucose derivatives 8 and 9, respectively, we determined their relative  $pK_a$  values and recorded their infrared spectra.

The relative basicities and infrared spectral data of the ylids are given in Table II. In this Table, the ylids are arranged in order of decreasing basicity. There is, apparently, no definite correlation between the  $pK_a$  values and the shift in the carbonyl stretching vibration of the various phosphorus ylids. Similarly, comparison of the data given in Tables I and II does not reveal any significant trend. It therefore appears that the reaction between the ylids 1–7 and the *aldehydo* sugars 8 and 9 is a rather complex reaction that is partially dependent on factors other than the basicity and nucleophilicity of the ylid; steric hindrance (by substituents on the carbohydrate and on the ylid) probably plays a significant role in the overall rate of the Wittig reaction.

Ylid	pKa	$v_{max}^{Nujol}$ (cm <sup>-1</sup> ) for C=0	
3	10.6	1626	
4	8.8	1615	
5	7.7		
1	7.1	1620	
2	6.5	1640	
6	6.4	1525ª	
7	6.0	1590	

TABLE II Relative basicities and infrared spectra (stretching frequency of C=0) of ylids 1–7

<sup>a</sup>Probably the C-O stretch of an enolate ion.

#### EXPERIMENTAL

Melting points were determined with a Thomas-Hoover melting-point apparatus and are corrected. The elemental analyses were performed by Midwest Microlab Inc., Indianapolis, Indiana. A Beckman IR-8 spectrophotometer was used for recording the i.r. spectra of Nujol mulls of the compounds.

Determination of relative  $pK_a$ 's (Table II). — The method of Speziale and Ratts<sup>10</sup> was used for determining the relative  $pK_a$ 's by potentiometric titration (Beckman pH meter and a mini-electrode) of methanolic solutions of the ylids with hydrochloric acid.

General procedure for Wittig reactions. — A solution of equimolar amounts ( $\sim$ 6 mmoles) of the appropriate ylid and the aldehydo sugar in tetrahydrofuran (100 ml) was boiled for 2 h under reflux, and evaporated to dryness under diminished pressure. The residue was dissolved in the minimal volume of absolute ethanol or butyl ether, and on cooling the solution to about 10°, the product crystallized, leaving the triphenylphosphine oxide (by-product) in solution. Filtration of the suspension, followed by recrystallization from the same solvent afforded the analytical samples.

2,4:3,5-Di-O-benzylidene-1-deoxy-1-(2,5-dioxo-3-pyrrolidinylidene)-D-ribitol (10), m.p. 194-195°; lit.<sup>2</sup> m.p. 194-195°.

2,4:3,5-Di-O-benzylidene-1-deoxy-1-(2,5-dioxo-1-phenyl-3-pyrrolidinylidene)-D-rıbitol (11), m.p. 212–213°; lit.<sup>2</sup> m.p. 212–213°.

4,6:5,7-Di-O-benzylidene-2,3-dideoxy-D-ribo-hept-2-enonamide (12), m.p. 260°.

Anal. Calc. for C<sub>21</sub>H<sub>21</sub>NO<sub>5</sub>: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.80; H, 5.63; N, 3.79.

Ethyl 4,6:5,7-di-O-benzylidene-2,3-dideoxy-D-ribo-hept-2-enonate (13), m.p. 160–161°.

Anal. Calc. for C<sub>23</sub>H<sub>24</sub>O<sub>6</sub>: C, 69.68; H, 6.10. Found: C, 69.54; H, 6.13.

4,6:5,7-Di-O-benzylidene-2,3-dideoxy-D-*ribo*-hept-2-enononitrile (14), m.p. 169–171°.

Anal. Calc. for C<sub>21</sub>H<sub>19</sub>NO<sub>4</sub>: C, 72.19; H, 5.48; N, 4.00. Found: C, 71.80; H, 5.55; N, 3.92.

5,7:6,8-Di-O-benzylidene-1,3,4-trideoxy-D-ribo-oct-3-enulose (15), m.p. 196-197°.

Anal. Calc. for C22H22O5: C, 72.11; H, 6.05. Found: C, 71.89; H, 6.04.

# 4,6:5,7-Di-O-benzylidene-2,3-dideoxy-1-C-phenyl-D-ribo-hept-2-enose (16), m.p. 186-187°.

Anal. Calc. for C<sub>27</sub>H<sub>24</sub>O<sub>5</sub>: C, 75. 68; H, 5.64. Found: C, 75.84; H, 5.69.

2,3-Dideoxy-D-gluco-oct-2-enonamide 4,5,6,7.8-pentaacetate (17), m.p. 130-131°.

Anal. Calc. for C<sub>18</sub>H<sub>25</sub>NO<sub>11</sub>: C, 50.11; H, 5.84; N, 3.24. Found: C, 50.07; H, 5.60; N, 3.26.

Ethyl 2,3-dideoxy-D-gluco-oct-2-enonate 4,5,6,7.8-pentaacetate (18), m.p. 133-135°; lit.<sup>11</sup> m.p. 133-134.5°.

2,3-Dideoxy-D-gluco-oct-2-enononitrile 4,5,6,7,8-pentaacetate (19), m.p. 125-127°.

Anal. Calc. for C<sub>18</sub>H<sub>23</sub>NO<sub>10</sub>: C, 52.42; H, 5.62; N, 3.39. Found: C, 52.28; H, 5.48; N, 3.32.

2,3-Dideoxy-1-C-phenyl-D-gluco-oct-2-enose 4,5,6,7,8-pentaacetate (20), m.p. 93-94°.

Anal. Calc. for C24H28O11: C, 58.53; H, 5.73. Found: C, 58.27; H, 5.69.

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#### REFERENCES

- 1 R. E. HARMON, G. WELLMAN, AND S K. GUPTA, Abstr. Papers Amer. Chem. Soc. Meeting, 158 (1969), CARB 027.
- 2 R. E. HARMON, G. WELLMAN, AND S. K. GUPTA, Carbohyd. Res., 11 (1969) 574.
- 3 N. K. KOCHETKOV AND B A. DMITRIEV, Tetrahedron, 21 (1965) 803.
- 4 N. K. KOCHETKOV AND B. A DMITRIEV, Dokl Akad. Nauk SSSR, 151 (1963) 106.
- 5 C. F. HAUSER, T. W. BROOKS, M. L. MILES, M. A. RAYMOND, AND G. B. BUTLER, J. Org Chem., 28 (1963) 372.
- 6 E. HEYDA AND S. THEODOROPULOS, Tetrahedron, 24 (1968) 2241.
- 7 A. W. JOHNSON, Ylid Chemistry, Academic Press, London, 1966, p. 52.
- 8 D. S. POTGIETER AND D. L. MACDONALD, J. Org. Chem, 26 (1961) 3934.
- 9 M. L. WOLFROM AND A THOMPSON, Methods Carbohyd. Chem., 2 (1963) 427.
- 10 A. J. SPEZIALE AND K. W. RATTS, J. Amer. Chem. Soc., 85 (1963) 2790
- 11 YU. A. ZHDANOV, G. N. DOROFEENKO, AND L. A. UZLOVA, Zh Obshch. Khim., 35 (1965) 181.

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